UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/037,064	11/07/2001	Friederike Zahm	9526	6197

151 7590 03/12/2003

HOFFMANN-LA ROCHE INC.
PATENT LAW DEPARTMENT
340 KINGSLAND STREET
NUTLEY, NJ 07110

EXAMINER	
JIANG, SHAOJIA A	

ART UNIT	PAPER NUMBER
1617	7

DATE MAILED: 03/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/037,064	ZAHM, FRIEDERIKE	
	Examiner	Art Unit	
	Shaojia A. Jiang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. *09/317,688* .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5 and 6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This application is a continuation of Serial No. 09/317,688 (now abandoned), which claims the foreign priority EPO 98110433.4 under 35 U.S.C. 119(a)-(d). The certified copy has been filed in the parent application 09/317,688.

The form of the instant claims is objected to because of the following informalities: missing the phrase before the claims, "I (or we) claim," or "The invention claimed is". According to MEEP 608.01(m) "While there is no set statutory form for claims, the present Office practice is to insist that each claim must be the object of a sentence starting with "I (or we) claim," "The invention claimed is" (or the equivalent). Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "substantially" in claims 5 and 10 is a relative term which renders claims 5 and 10 indefinite. The expression "substantially all of the ribavirin" is not defined in the specification. Hence, one of ordinary skill in the art could not interpret the metes and bounds as to the recitation "substantially all of the ribavirin" in the claim.

Therefore, the scope of the claims is indefinite as to how much ribavirin to be administered would be considered to be "substantially all of the ribavirin" herein.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grint et al. (EP 0707855 A2, PTO-1449 submitted December 17, 1999 in the parent application 09/317,688) in view of Bailon et al. (EP 0809996 A2, PTO-1449 submitted August 17, 1999).

Grint et al. discloses a method for treating chronic hepatitis C infections comprising administering concurrently an effective amount of alpha interferon (IFN-alpha or INF-α) and an effective amount of ribavirin daily. See the abstract, col. 1 lines 31-38 and 51, col.2 line 5 in particular and claims 12-20. Grint et al. teaches that the combination therapy in treating chronic hepatitis C infections is considered to be more effective than either monotherapy and to reduce side effects associated with either compound (see col.1 lines 22-28 in particular). Grint et al. also disclosed the effective amounts of both alpha interferon (e.g., 1-2 million IU weekly or daily, see page 2 lines 52—53 in particular) and ribavirin (i.e., 400-1000 mg daily, within the instant claimed range of ribavirin) (see claims 15-16 in particular). Grint et al. further discloses that the

concurrent administration of alpha interferon and ribavirin may be daily or thrice weekly in the period from 6 to 12 months, e.g., at least one dose of ribavirin is administered within the same period of time that the patient administered alpha interferon. See col.2 lines 50-58, col.3 lines 10-26 and claim 20 in particular.

The prior art does not expressly disclose the employment of the particular alpha-interferon agents, the PEG-IFN-alpha conjugates, in combination with ribavirin in a method for treating chronic hepatitis C infections. The prior art does also not expressly disclose the effective amounts of the particular alpha-interferon agents, the PEG-IFN-alpha conjugates, in combination with ribavirin in a method for treating chronic hepatitis C infections.

Bailon et al. teaches that interferon, in particular INF-alpha2A, is known to be active against hepatitis (see page 2 lines 1-4). Bailon et al. discloses the particular alpha-interferon (IFN-alpha) agents, the PEG-IFN-alpha conjugates represented by the structural formula I, which obtained from conjugating IFN-alpha and PEG (well known as peglated). See the abstract, page 2 lines 6, 27, 37-50 and claims 1-14. Bailon et al. also discloses that the PEG-IFN- alpha conjugates have the same therapeutic usefulness as IFN- alpha. Moreover, Bailon et al. discloses that PEG-IFN-alpha conjugates are much better than IFN- alpha alone without PEG attached, since PEG-IFN- alpha conjugates increases stability, solubility and circulating half-time of IFN-alpha, and reduces immunogenicity of IFN-alpha. As a result, the antiviral activity of IFN-alpha is improved, compared to an IFN-alpha without a PEG conjugated. See page 2 lines 5-6, lines 31 to page 3 lines 45. Bailon et al. discloses that the effective amounts

of PEG-IFN-alpha conjugates to be administered are 30-300 μg (micro gram or mcg) per week, (within the instant claims). See page 9 lines 28-29 and 41-45.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ the particular alpha- interferon agents, the PEG-IFN-alpha conjugate in an effective amount, in combination with an effective amount of ribavirin in a method for treating chronic hepatitis C infections.

One having ordinary skill in the art would have been motivated to employ the particular PEG-IFN-alpha conjugates herein in combination with ribavirin in a method for treating chronic hepatitis C infections because the combination of IFN-alpha and ribavirin in their effective amounts are known to be useful in a method for treating chronic hepatitis C infections according to Grint et al. More importantly, the activity of PEG-IFN-alpha conjugates of the instant claim are known to be improved to have more advantages or benefits, i.e., the increase in stability, solubility and circulating half-time of IFN-alpha, and reducing immunogenicity of IFN-alpha, than an IFN-alpha without a PEG conjugated according to Bailon et al. Therefore, one of ordinary skill in the art would have reasonably expected that the employment of the PEG-IFN-alpha conjugates in replacing IFN-alpha in combination with ribivirin would improve the therapeutic effects against chronic hepatitis C infections because of the greater activity provided by the pegylated IFN-alpha.

Additionally, one of ordinary skill in the art would have been motivated to optimize the effective amounts of the PEG-IFN-alpha conjugate and ribavirin in a composition and dosage regimen since the effective amounts of these agents are

known and the optimization of known amounts of active agents to be administered and dosage regimen is considered well within the skill of artisan. It has been held that it is within the skill in the art to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980).

Claims 6-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grint et al. (EP 0707855 A2) in view of Bailon et al. (EP 0809996 A2).

Grint et al. discloses a method for treating chronic hepatitis C infections comprising administering concurrently an effective amount of alpha interferon (IFN-alpha or INF-α) including the preferred interferon alpha-2A (INF-alpha2A) (see col.1 line 51 and col.2 line 5 in particular) and an effective amount of ribavirin daily. See the abstract, col. 1 lines 31-38 and claims 14-20. Grint et al. teaches that the combination therapy in treating chronic hepatitis C infections is considered to be more effective than either monotherapy and to reduce side effects associated with either compound (see col.1 lines 22-28 in particular). Grint et al. also disclosed the effective amounts of both alpha interferon interferon (e.g., 1-2 million IU weekly or daily, see page 2 lines 52-53 in particular) and ribavirin (i.e., 400-1000 mg daily which may be administered once per day in a single dose or in divided doses, within the instant claimed range of ribavirin) (see col.3 lines 8-11 and claims 15-16 in particular). Grint et al. further discloses that the concurrent administration of alpha interferon and ribavirin may be daily or thrice weekly in the period from 6 to 12 months (48 weeks), e.g., at least one dose of ribavirin is

administered within the same period of time that the patient administered alpha interferon. See col.2 lines 50-58, col.3 lines 10-26 and claim 20 in particular.

The prior art does not expressly disclose the employment of the particular alpha-2A interferon (IFN-alpha2A) agents, the PEG-IFN-alpha2A conjugates represented by the structural formula of the instant claim in combination with ribavirin in a method for treating chronic hepatitis C infections. The prior art does also not expressly disclose the effective amounts of the particular alpha-interferon agents, the PEG-IFN-alpha2A conjugates, in combination with ribavirin in a method for treating chronic hepatitis C infections.

Bailon et al. teaches that interferon, in particular INF-alpha2A, is known to be active against hepatitis (see page 2 lines 1-4). Bailon et al. discloses the particular alpha-interferon (IFN-alpha) agents, the PEG-IFN-alpha conjugates represented by the structural formula I including PEG-IFN-alpha2A conjugates herein (see especially page 2 line 37-50 and 55-58, page 9 lines 22, 29, 34, 42 and 44). See also the abstract, page 2 lines 6, 27, and claims 1-14. Bailon et al. discloses that the PEG-IFN-α conjugates including PEG-IFN-alpha2A conjugates have the same therapeutic usefulness as IFN-alpha or IFN-alpha2A. Moreover, Bailon et al. discloses that PEG-IFN- alpha2A conjugates are much better than IFN-alpha2A alone without PEG attached, since PEG-IFN- alpha2A conjugates increases stability, solubility and circulating half-time of IFN-alpha2A, and reduces immunogenicity of IFN-alpha2A. As a result, the antiviral activity of IFN-alpha2A is improved, compared to an IFN-alpha2A without a PEG conjugated. See page 2 lines 5-6, lines 31 to page 3 lines 45. Bailon et al. discloses that the

effective amounts of PEG-IFN-alpha2A conjugates to be administered are 30-300 μg (micro gram or mcg) per week, (within the instant claims). See page 9 lines 28-29 and 41-45.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ the particular alpha-2A interferon (IFN-alpha2A) agents, the PEG-IFN-alpha2A conjugate represented by the structural formula of the instant claim in an effective amount, in combination with an effective amount of ribavirin in a method for treating chronic hepatitis C infections.

One having ordinary skill in the art would have been motivated to employ the particular PEG-IFN-alpha2A conjugates herein in combination with ribavirin in a method for treating chronic hepatitis C infections because the combination of IFN-alpha2A and ribavirin in their effective amounts are known to be useful in a method for treating chronic hepatitis C infections according to Grint et al. More importantly, the activity of PEG-IFN-alpha2A conjugates of the instant claim are known to possess more advantages or benefits, i.e., the increase in stability, solubility and circulating half-time of IFN-alpha2A alone, and reducing immunogenicity of IFN-alpha2A, than an IFN-alpha2A without paglating based on the disclosure of Bailon et al. Therefore, one of ordinary skill in the art would have reasonably expected that the employment of the PEG-IFN-alpha2A conjugates in replacing IFN-alpha2A in combination with ribivirin would improve the therapeutic effects against chronic hepatitis C infections because of the greater activity provided by the pegylated IFN-alpha2A.

Additionally, one of ordinary skill in the art would have been motivated to optimize the effective amounts of the PEG-IFN-alpha conjugate and ribavirin in a composition and dosage regimen since the effective amounts of these agents are known and the optimization of known amounts of active agents to be administered and dosage regimen is considered well within the skill of artisan. It has been held that it is within the skill in the art to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980).

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

In view of the rejections to the pending claims set forth above, no claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (703) 305-1008. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (703) 305-1877. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-1235.

S. Anna Jiang, Ph.D.
Patent Examiner, AU 1617
March 6, 2003